REMARKS/ARGUMENTS

Claims 1-2, 4, 6-8, 18 and 22-33 have been withdrawn. Claims 3, 5, 9-17 and 19-21 are under consideration. Claims 3, 5, 9, 13, 15 and 20-21 have been amended. Claims 3 and 5 have been amended to depend from elected claims 11 and 13, respectively. Support for amended claims 3 and 5 can be found at page 38, lines 21-22. Claim 9 was amended to independent claim format. Support for amended claim 13 can be found at page 7, lines 17-20. Claim 15 was amended to correct a typographical error. Support for amended claims 20-21 can be found at page 18, lines 21-25.

Applicants note the lack of a shortened statutory period for reply and, therefore, believe the statutory period of six months applies. Nevertheless, Applicants have filed this response before expiration of the three month period, thus avoiding any delay in prosecution.

Restriction

Applicants have elected the claims of Group II (claims 9-17 and 19-21) and the species SEQ ID NO:1 with traverse. Applicants point out that that elected claims read on human Ozz nucleic acid (SEQ ID NO:3) as well as mouse Ozz nucleic acid (SEQ ID NO:1). Applicants reserve the right to claim a reasonable number of species, including mouse and human, upon allowance of a generic claim.

Claim Objections

Claim 9 has been objected to because it depends from non-elected claim 1. Claims 12 and 20-21 have been objected to because they recite the non-elected nucleotide sequence of SEQ ID NO:3.

The claim objections have been obviated or overcome. Claim 9 has been amended to independent claim format. Claims 12 and 20-21 claim a non-elected species, but Applicants are entitled to maintain claims directed to multiple species of the invention even though one species was elected for purposes of search.

Rejection under 35 U.S.C. §101

Claims 9-17 and 19-21 have been rejected under 35 U.S.C. §101 as not supported by a credible asserted utility or a well established utility. This rejection is respectfully traversed.

One specific, substantial utility for the Ozz nucleic acids is for making Ozz protein, which in turn is useful for preparing reagents for the detection of conditions associated with muscle damage. "[T]he presence of Ozz in blood or a blood fraction (serum, plasma) indicates muscle tissue damage, *e.g.,* ischemia associated with either unstable angina, myocardial infarction, or both..." (p. 34, ll. 7-10). The claimed nucleic acids provide for manufacture of recombinant Ozz protein, which provides an antigen source for preparing antibodies and a positive control for assays.

A second credible asserted utility is the use of Ozz protein relates to its distribution in certain disease states, such as galactosialidosis. Using anti-mouse Ozz antibodies, it was shown that Ozz accumulated in the region of the atrial cardiomyocytes surrounding the nucleus in normal human atria. The amount and distribution of Ozz was altered in the atria of patients with galactosialidosis. (page 44, lines 1-13). Thus, as the specification discloses, "altered Ozz protein levels and localization can be detected to diagnose diseases associated with altered Ozz protein expression and localization" (page 34, lines 11-12). As noted above, the claimed nucleic acids are a source for preparing Ozz protein for immunization and control.

A third credible asserted utility is as a research reagent. As the specification states, "nucleotide sequences derived from the gene encoding Ozz, and peptide sequences derived from Ozz, are useful targets to identify drugs that are effective in treating myogenesis disorders" (p.29, lines 25-28). This utility is credible because *in vitro* tests showed a sharp increase in Ozz protein upon myoblast differentiation, which coincided with the appearance of myosin and the decrease of myogenin (known markers for muscle differentiation) (p. 40, l. 27- p.41, l.6). An important attribute for a drug effective to treat myogenesis disorders is targeting of the diseased tissue, differentiating muscle cells. Thus, screening for molecules that target nucleotide sequences from the gene encoding Ozz or peptide sequences derived from Ozz is useful to identify drugs that have the attribute of targeting differentiating muscle cells. Such screening reagents are valuable, i.e., constitute real, credible, and substantial utility.

The assertion of one credible utility or a well established utility meets the utility requirement under 35 U.S.C. §101. See e.g., *Raytheon v. Roper,* 724 F.2d 951, 958 (Fed. Cir. 1983), *cert denied*, 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. 101 is clearly shown."). As described above, Applicants exceeded the statutory requirement by asserting three credible utilities and, thus, meet the utility requirement.

Rejection under 35 U.S.C. §112, First Paragraph, Enablement

Claims 9-17 and 19-21 have been rejected under 35 U.S.C. §112, first paragraph because, according to the Examiner, the claimed invention is not supported by either a credible asserted utility or a well established utility and, therefore, one skilled in the art would not know how to use the claimed invention. This rejection is respectfully traversed.

A lack of utility rejection under 35 U.S.C. §101 also creates a rejection under 35 U.S.C. §112, first paragraph. See *In re Brana,* 51 F.3d 1560 (Fed. Cir. 1995). However, a lack of utility rejection under 35 U.S.C. §112, first paragraph should not be imposed or maintained unless an appropriate basis exists for imposing the lack of utility rejection under 35 U.S.C. §101. See MPEP 2107.01(IV). The remarks in the section immediately above point out the utility of the claimed invention under 35 U.S.C. §101 as disclosed in the specification. Thus, the rejection under 35 U.S.C. §112, first paragraph, enablement should be withdrawn.

Having knowledge of the disclosed utility, one skilled in the art would know how to use the claimed invention by, for example, applying the disclosed Methods of Diagnosis, Nucleic Acid Assays, and Protein Assays (page 34, line 1 - page 35, line 18).

Rejection under 35 U.S.C. §112, First Paragraph, Written Description

Claims 20-21 have been rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not conveyed in the specification as to reasonably convey to one skilled in the art that the inventor, at the time the application was filed, had possession of the claimed invention. According to the Examiner, there is no disclosure of any particular structure to function/activity relationship in the disclosed species, and the specification fails to describe additional representative species of these polynucleotides by any identifying structural characteristics or properties for which no predictability of structure is apparent. This rejection is respectfully traversed.

Amended claim 20 has been amended to include the limitation "at least ten consecutive bases." Support for this amendment can be found at page 18, lines 21-25, "a nucleic acid, generally of at least 10...nt...that is hybridizable..." Thus, the specification supports an

isolated nucleic acid having only ten nucleotides, in which case the nucleotides must be consecutive.

The specification discloses: oligonucleotide primers and probes (page 7, lines 7-11); oligonucleotides having at least 10 nucleotides (page 18, lines 21-24); labeled oligonucleotides used as a probe (page 18, lines 21-27); and oligonucleotides used as PCR primers (page 18, lines 21-29). Additional disclosure of screening for the presence of a gene encoding Ozz using an oligonucleotide probe can be found at page 20, lines 20-30.

Thus, the specification provides a sufficiently detailed disclosure of physical characteristics (an isolated nucleic acid of at least ten consecutive bases that hybridizes under stringent conditions with a nucleic acid having a nucleotide sequence as depicted in SEQ ID NO:1 or SEQ ID NO:3, with the proviso that the nucleic acid is not a PPCA exon Ia) and functional characteristics (i.e., these oligonucleotides can be primers and/or probes, see immediately preceding paragraph) to convey to a person skilled in the art that Applicant was in possession of the invention. Accordingly, the Examiner should withdraw this rejection.

Rejection under 35 U.S.C. §112, Second Paragraph

Claim 20 has been rejected under 35 U.S.C. §112, second paragraph, as indefinite because (1) the meaning of the phrase "ten bases" is not known, (2) the specific hybridization conditions have not been recited, and (3) the specific nucleotide sequence/structure of the "PPCA exon Ia" is not known and not recited. This rejection is respectfully traversed.

Claim 20 has been amended to include the limitation "at least ten consecutive nucleotides" and, thus, the rejection based on indefiniteness of the phrase "ten bases" is overcome.

Claim 20 reads "hybridizes under stringent conditions." "High stringency" is defined in the specification as "hybridization . . . at 68°C in 0.2XSSC, at 42°C in 50% formamide, 4XSSC, or under conditions that afford levels of hybridization equivalent to those observed under either of these two conditions." (page 18, lines 17-20)

The structure of PPCA exon Ia was known. For example, see Rottier et al., DNA Cell Biol. 1997;16(5):599-610 ("Rottier") (specification, page 4, lines 17-25). Rottier discloses: "mouse exon Ia position 11-30, GGAATTCGATGCGCAGATAGGGTTCAA-3'" (Rottier, page 600, 2nd column, 2nd full paragraph).

In view of the foregoing, the claims are clear and definite because Applicants have defined the terms explicitly. The skilled artisan would understand these terms without difficulty.

Rejection under 35 U.S.C. §102(b)

Claims 9-11 have been rejected under 35 U.S.C. §102(b) as anticipated by Nakamura et al., Oncogene 1998;16(8):1009-19 ("Nakamura"). The Examiner interpreted the claims to encompass any nucleic acid encoding any protein involved in development and function of muscle with homology with Drosophila *neu.*

The Examiner has incompletely defined the claimed protein "Ozz". Ozz protein has a characteristic tissue-specific expression. For example, the specification states that Ozz mRNA and Ozz protein were only observed in heart and skeletal muscle using routine assays such as Northern analysis and Western analysis. Page 8, lines 1-5. Nakamura discloses a human neuralized protein ("h-neu") with homology to the Drosophila neuralized protein ("d-neu"). In contrast to Ozz, h-neu transcription was detected in normal brain tissues and astrocytoma tissue (a brain tumor)

using Northern blot hybridization (page 1011, column 2, last paragraph to page 12, column 1, first paragraph). Thus, the nucleic acid disclosed by Nakamura does not encode an Ozz protein.

Further, Nakamura hypothesizes that the h-neu gene plays a role in the determination of cell fate in the central nervous system (Nakamura, abstract), a role highly unlikely to be played by Ozz protein, which is present in muscle, and not nervous, tissue.

Because Nakamura does not teach the claimed invention, it cannot anticipate claims 9-11. The Examiner should withdraw this rejection.

Rejection under 35 U.S.C. §102(b)

Claim 13 has been rejected under 35 U.S.C. §102(b) as anticipated by Prinos et al., Tetrology 1998;57(2):108 ("Prinos"). The Examiner interpreted the claims to encompass any nucleic acid encoding any protein involved in development and function of muscle with homology to Drosophila *neu*. According to the Examiner, Prinos discloses a cDNA for a mouse homolog of the Drosophila neuralized gene.

Claim 13 has been amended to expressly recite the implicit limitation that the Ozz protein has a molecular weight of about 30 kDa. Prinos discloses a nucleic acid encoding a polypeptide with a theoretical molecular weight of approximately 61.9 kDa. Prinos does not anticipate amended claim 13 because the polypeptide encoded by the nucleic acid disclosed in Prinos is more than twice the molecular weight of the Ozz protein encoded by the nucleic acid claimed in amended claim 13. Consequently, the Examiner should withdraw this rejection.

Rejection under 35 U.S.C. §102(b)

Claim 20 has been rejected under 35 U.S.C. §102(b) as anticipated by Lee et al. According to the Examiner, this reference discloses "a nucleic acid which is expected to hybridize

to SEQ ID NO: 1 because no specific hybridization conditions have been recited." As noted above, claim 20 recites "stringent conditions," which are "hybridization . . . at 68°C in 0.2XSSC, at 42°C in 50% formamide, 4XSSC, or under conditions that afford levels of hybridization equivalent..." (page 18, lines 17-20). Under high stringency hybridization conditions, only nucleotides having the highest degree of sequence similarity will hybridize (page 17, line 32 to page 18, line 20). Thus, this rejection is overcome because there is no expectation that the nucleic acid disclosed by Lee et al. will hybridize under stringent conditions to the nucleic acid of the present invention.

Conclusion

In view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

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Respectfully submitted,

By _____

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